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Formic Acid Reduction. XXVI.¹⁾ α,β -Reduction of Conjugated Nitriles with Formic Acid

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Formic acid reduction selective at α,β -double bond of conjugated nitriles is described. Selective reduction of carbon-carbon double bond conjugated with two cyano groups or with both cyano and other electron-withdrawing group has been demonstrated with several examples by the use of the TEAF reagent (triethylamine-formic acid azeotrope) in N,N-dimethylformamide.

Keywords— α,β -unsatd. nitriles; formic acid redn.; formic acid-triethylamine azeotrope; selective redn.; base-induced dimerization; dimerization; decompn. of formic acid

Methods now available for reduction of α,β -unsaturated nitriles include catalytic hydrogenation,³⁾ photochemical reduction with organostannic hydride,⁴⁾ reduction with magnesium in methanol⁵⁾ and sodium borohydride reduction.⁶⁾

The preceding communication¹⁾ described our finding that formic acid affects selective reduction of the carbon-carbon double bonds conjugated with the functional groups such as cyano, nitro and sulfonyl groups. First, taking up the double bonds conjugated with cyano group, we wish to disclose the details of its formic acid reduction.

Experimental data of the formic acid reduction of benzylidenemalononitrile (Ia) are shown in Table I. It was attractive that the use of N,N-dimethylformamide (DMF) as a solvent highly promotes the reduction not only with the triethylamine-formic acid azeotrope (TEAF)⁷⁾ but also with formic acid. Using the most favored TEAF-DMF medium formic acid reductions of a variety of α,β -unsaturated cyano compounds were then carried out. Results are summarized in Table II.

The conjugated double bonds which are able to undergo the reduction should be conjugated with two cyano groups or with both cyano group and one of the other electron-withdrawing groups such as carboethoxy and sulfonyl. Reactivities with respect to X group in $\text{PhCH}=\text{C}(\text{CN})\text{X}$ are deduced to be in the order of $\text{CN} > \text{PhSO}_2 > \text{CO}_2\text{Et}$. Benzylidenephénylacetonitrile and 1-cyanocyclohexene did not undergo the reduction even on heating up to 145–150°, resulting in recovery of the starting nitriles. In the latter case, it was emphasized that decomposition of formic acid into carbon dioxide and hydrogen proceeded with considerable

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TABLE I. Formic Acid Reduction of Benzyldenemalononitrile

	Reagent	Solvent ^{a)}	Reaction temp. (°C)	Reaction time (hr)	Yield (%) ^{b)}
1	99% HCO ₂ H	99% HCO ₂ H	100—105 ^{c)}	5	0
2	99% HCO ₂ H ^{d)}	DMF	120—130	12	81
3	99% HCO ₂ H ^{d)}	Pyridine	88—91	5.5	58
4	TEAF	TEAF	60	2.5	90
5	TEAF ^{d)}	DMF	25—30	2	91
6	TEAF ^{d)}	THF	55—57	2	74

a) 40 ml for 0.02 mol of benzyldenemalononitrile.

b) Based on benzyldenemalononitrile isolated.

c) At this temperature no evolution of carbon dioxide was observed.

d) Benzyldenemalononitrile (0.02 mol)/HCO₂H=1/3 in molar proportion.TABLE II. Formic Acid Reduction^{a)} of Carbon-Carbon Double Bonds Conjugated with Cyano Group

Compd. No.	R ₁	R ₂	X	Reaction temp. (°C) ^{b)}	Reaction time (hr)	Yield (%) ^{c)}
Ia	Ph	H	CN	25—30	2.0	91
Ib	Ph	H	CO ₂ Et	50—55	2.0	84
Ic	Ph	H	SO ₂ Ph	45—50	1.5	93
Id	Ph	CH ₃	CO ₂ Et	75—80	8.5	85
Ie	Ph	C ₂ H ₅	CN	75—80	5.0	77
If	Ph	C ₂ H ₅	CO ₂ Et	75—80	7.0	89
Ig	Ph	CH ₂ Ph	CN	65—70	2.0	90
Ih	C ₂ H ₅	C ₂ H ₅	CN	28—32	3.0	65
Ii	—CH ₂ (CH ₂) ₃ CH ₂ —		CN	40—45	2.0	99

a) Substrate: 0.02 mol, TEAF: 5.2 g (0.06 mol as HCO₂H), DMF: 40 ml.

b) Temperature effecting considerable evolution of carbon dioxide.

c) Based on the product isolated.

rapidity at above 125°, indicating that 1-cyanocyclohexene is highly efficient as an organic catalyst in the decomposition of formic acid. In the cases of 1-methylpropyldenemalononitrile (III) and 1-phenylethyldenemalononitrile (V) the reaction was favored by a base-catalyzed dimerization rather than the reduction. The base-catalyzed dimerization of III and V had been reported to occur in the other reactions.^{8,9)} Previously, the dimer from III

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has been assigned as the structure of IV⁸⁾ and very recently that from V as VI.⁹⁾ Nuclear magnetic resonance (NMR) spectra of the products obtained were well in agreement with the data reported for IV and VI.

3-Cyanocoumarin (VIIa) and its 4-methyl derivative (VIIb) were reduced at rather higher temperature, 115–130°, to give 3-(*o*-hydroxyphenyl)propionitrile (VIIIa) and 3-(*o*-hydroxyphenyl)butyronitrile (VIIIb), respectively, in good yields. Process of this reaction may involve hydrolysis and decarboxylation. Rapid raising to the reaction temperature was necessary in order to promote the reduction. Contrary to the above reductions, 3-cyano-4,6-dimethyl-2-pyridone and its N-methyl derivative were not reduced even at 145–150°.

Experimental¹⁰⁾

α,β -Unsaturated Nitriles—Compounds, (Ia–i), 1-methylpropylidenemalononitrile and 1-phenylethylidenemalononitrile were prepared by Cope condensation of corresponding nitriles with ketones or aldehydes in benzene using ammonium acetate–acetic acid as catalyst. Others were prepared according to the methods described in the literature cited. Compound, Ia: needles (MeOH), mp 82–84° (lit.¹¹⁾ mp 83.5–84°, Ib: prisms (EtOH), mp 46–47° (lit.¹²⁾ mp 51°, Ic: prisms (AcOH), mp 133–134° (lit.¹³⁾ mp 140°, Id: colorless oil, bp 113–118°/0.02 mmHg (lit.¹⁴⁾ bp 134–135°/2 mmHg, Ie: colorless prisms (EtOH), mp 68–69° (lit.¹⁵⁾ mp 69–70°, If: colorless oil, bp 122–130°/0.08 mmHg (lit.¹⁴⁾ bp 138–140°/2 mmHg, Ig: needles (EtOH), mp 80–81°, *Anal.* Calcd. for C₁₇H₁₂N₂: C, 83.58; H, 4.95; N, 11.47. Found: C, 83.78; H, 5.00; N, 11.74. Ih: colorless liquid, bp 110°/0.4 mmHg (lit.⁸⁾ bp 150°/19 mmHg, Ii: colorless liquid, bp 113°/4 mmHg (lit.¹⁶⁾ bp 137–138°/10 mmHg, benzylidenephénylacetonitrile (EtOH), mp 85–87° (lit.¹⁷⁾ mp 88°, 1-cyanocyclohexene: colorless liquid, bp 56–61°/3 mmHg (lit.¹⁸⁾ bp 77–87°/12 mmHg, 1-methylpropylidenemalononitrile: colorless liquid, bp 66–75°/0.09 mmHg (lit.¹⁹⁾ bp 82°/4 mmHg, 1-phenylethylidenemalononitrile: mp 93–95° (lit.¹⁵⁾ mp 93–94°, 3-cyanocoumarin: pale yellow pillar (EtOH), mp 182–184° (lit.²⁰⁾ mp 184–185°, 3-cyano-4-methyl-coumarin: colorless needles (aqueous acetone), mp 188–190° (lit.²¹⁾ mp 191–192°, 3-cyano-4,6-dimethyl-2-pyridone: colorless powder, mp 284–286° (lit.²²⁾ mp 288–289°, 3-cyano-1,4,6-trimethyl-2-pyridone: colorless prisms (EtOH), mp 196–198° (lit.²³⁾ mp 203–204°).

Formic Acid Reduction of α,β -Unsaturated Cyano Compounds (Ia–i) **General Procedure**—A mixture of 40 ml of DMF, 0.02 mol of α,β -unsaturated cyano compound (Ia–i) and 5.2 g (0.06 mol based on HCO₂H) of TEAF was stirred at appropriate temperature (see Table II). Dry air free from CO₂ was introduced in

- 10) All melting points and boiling points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-G2 spectrophotometer. NMR spectra were taken with a JEOL-C-60-H spectrophotometer (at 60 MHz). Chemical shift values are given in δ (ppm) relative to tetramethylsilane as an internal standard. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, p=pentuplet, sx=sextuplet, m=multiplet.
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order to check evolution of CO₂ by saturated Ba(OH)₂ solution. After CO₂ evolution ceased, the reaction mixture was poured into 40 ml of ice-water and a liberated oily material was extracted with benzene and the benzene extract was washed and dried over anhydrous MgSO₄. Evaporation of benzene under reduced pressure gave the reduction product. Recrystallization or distillation under reduced pressure gave pure reduction products. In the cases of Ig, Ih and Ii, the products were purified through chromatography on silica gel column using hexane-benzene as an eluent. Physical and analytical data of the reduction products are summarized in Table III.

Formic Acid Reduction of 3-Cyanocoumarin (VIIa) and Its 4-Methyl Derivative (VIIb)—To a preheated solution of 10.4 g of TEAF in 20 ml of DMF 0.04 mol of VIIa or VIIb was added with stirring in three portions.

TABLE III. Physical and Analytical Data of the Reduction Products

$\begin{array}{c} \text{R}_1 \backslash \text{CHCH} \text{CN} \\ \text{R}_2 / \quad \backslash \text{X} \end{array}$						
Compd. No.	R ₁	R ₂	X	Appearance (recryst. solv.)	mp (°C) or bp (°C/mmHg) (lit.)	Formula
IIa	Ph	H	CN	Colorless prisms (EtOH)	87—88 (87—89) ^{a)}	C ₁₀ H ₈ N ₂
IIb	Ph	H	CO ₂ Et	Colorless oil	105—117/0.05 (165—173/15) ^{c)}	C ₁₂ H ₁₃ NO ₂
IIc	Ph	H	SO ₂ Ph	Colorless needles (CCl ₄)	85—85.5	C ₁₅ H ₁₃ NSO ₂
IId	Ph	CH ₃	CO ₂ Et	Colorless oil	115—120/0.07 (125—126/1.0) ^{d)}	C ₁₃ H ₁₅ NO ₂
IIf	Ph	C ₂ H ₅	CN	Colorless oil	105—113/0.12 (12—125/0.15) ^{b)}	C ₁₂ H ₁₂ N ₂
IIe	Ph	C ₂ H ₅	CO ₂ Et	Colorless oil	115—125/0.05 (118—120/0.5) ^{e)}	C ₁₄ H ₁₇ NO ₂
IIg	Ph	CH ₂ Ph	CN	Colorless cryst.	48—50.5	C ₁₇ H ₁₄ N ₂
IIh	C ₂ H ₅	C ₂ H ₅	CN	Colorless liquid	100—100.5/0.3	C ₈ H ₁₂ N ₂
IIi	CH ₂ (CH ₂) ₃	CH ₂	CN	Colorless liquid		C ₉ H ₁₂ N ₂

Compd. No.	Analysis (%)			IR (cm ⁻¹) CN CO (lit.)	α-H	NMR (δ) β-H (lit.)	J (Hz)
	Calcd. (Found)	C	H				
IIa		76.90 (76.65)	5.16 (5.08)	17.93 (18.01)	2200	3.92(t) (3.87(t)	7(6) ^{b)}
IIb		70.91 (70.72)	6.45 (6.30)	6.89 (6.78)	2250 1750	3.72(q)	6, 8
IIc		66.40 (66.42)	4.83 (4.81)	5.16 (5.15)	2230	4.09(q)	4, 11
IId		71.86 (72.10)	6.96 (7.05)	6.45 (6.64)	2230 1745	3.37—3.74(m)	
IIe		78.23 (78.42)	6.57 (6.70)	15.21 (15.32)	2230	3.90(d)	6, 8
IIf		72.70 (72.53)	7.41 (7.31)	6.06 (6.18)	2245(2245) ^{e)} 1740(1745)	3.90(q)	6, 8
IIg		82.90 (83.11)	5.73 (5.77)	11.37 (11.33)	2250	5.17(d)	7
IIh		70.55 (70.70)	8.88 (8.84)	20.57 (20.62)	2250	3.85(d)	5
IIi		72.94 (72.78)	8.16 (7.83)	18.90 (18.57)	2250	3.60(d)	6

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d) W. A. Mosher, P. W. Berger, A. P. Foldi, J. E. Gardner, T. J. Kelly, and C. Nebel, *J. Chem. Soc. (C)*, **1969**, 121.

e) R. L. Huang, Chong-Oon Ong, and S. H. Ong, *J. Chem. Soc., (C)*, **1968**, 2217.

During the addition temperature was kept at 115–125° in the former case and 125–130° in the latter case. Heating and stirring were continued until evolution of CO₂ almost ceased. The reaction solution was concentrated under reduced pressure to remove DMF and excess TEAF. The resulting residue was dissolved in benzene and the benzene solution was washed with water and dried over anhydrous MgSO₄. Evaporation of benzene and distillation of the residual oil under reduced pressure gave an oily reduction product VIIIa (bp 147–150°/0.7 mmHg) or VIIIb (bp 140–143°/0.05 mmHg), respectively. The latter was purified through silica gel column chromatography (2×25 cm) using benzene–hexane (50/1) as an eluent.

VIIIa: Colorless oil. Yield, 80%. IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3370 (OH), 2250 (CN). NMR (CDCl₃) δ : 2.45–3.10 (4H, m, -CH₂CH₂-), 6.20 (1H, broad, OH), 6.67–7.25 (4H, m, C₆H₄).

VIIIb: Colorless oil. Yield, 70%. IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3400 (OH), 2250 (CN). NMR (CDCl₃) δ : 1.44 (3H, d, CH₃CH<, $J=8.0$ Hz), 2.68 (1H, d, >CHC- $\overset{\text{Ha}}{\underset{\text{Hb}}{\text{C}}}$ -, $J_{\text{Ha-Hc}}=8.0$ Hz), 2.70 (1H, d, >CHC- $\overset{\text{Ha}}{\underset{\text{Hb}}{\text{C}}}$ -, $J_{\text{Hb-Hc}}=6.0$ Hz), 3.54 (1H, sx, CH₃CH<, $J=8.0$ Hz), 5.80 (1H, broad, OH), 6.60–7.40 (4H, m, C₆H₄).

Structures of VIIIa and VIIIb were further confirmed by converting them into *p*-nitrobenzoates in a usual manner.

3-[O-(*p*-Nitrobenzoyloxy)phenyl]propionitrile: Colorless needles (EtOH), mp 108–109°. Anal. Calcd. for C₁₆H₁₂N₂O₄: C, 64.86; H, 4.08; N, 9.46. Found: C, 64.67; H, 4.15; N, 9.41. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 2225 (CN), 1730 (CO). NMR (CDCl₃) δ : 2.55–3.18 (4H, m, -CH₂CH₂-), 7.25–7.50 (4H, m, C₆H₄), 8.45 (4H, s, *p*-O₂N-C₆H₄-).

3-[O-(*p*-Nitrobenzoyloxy)phenyl]butyronitrile: Colorless oil. Anal. Calcd. for C₁₇H₁₄N₂O₄: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.60; H, 4.06; N, 8.79. IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 2240 (CN), 1745 (CO). NMR (CDCl₃) δ : 1.42 (3H, d, CH₃CH<, $J=7.0$ Hz), 2.60 (2H, d, -CH₂-, $J=7.0$ Hz), 3.30 (1H, p, CH₃CHCH₂-, $J=7.0$ Hz), 7.10–7.45 (4H, m, C₆H₄), 8.36 (4H, s, *p*-O₂N-C₆H₄-).

Reaction of 1-Methylpropylenemalononitrile (III) with TEAF—When 10.4 g (0.12 mol based on HCO₂H) of TEAF was added to a solution of 5.0 g (0.04 mol) of III in 80 ml of DMF, a reaction was started, but CO₂ evolution was almost negligible. The reaction mixture was stirred at 35–40° for 3 hr. By pouring the reaction mixture into ice-water, yellow precipitates were deposited and collected by filtration. Recrystallization from benzene gave colorless prisms of 2-amino-6-ethyl-4-ethylidene-6-methyl-2-cyclohexene-1,1,3-tricarbonitrile (IV), mp 163–165° (lit.⁸) mp 167–169°, yield, 3.7 g (74%). Anal. Calcd. for C₁₄H₁₆N₂: C, 69.97; H, 6.71; N, 23.32. Found: C, 69.92; H, 6.67; N, 23.30. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 3400, 3300, 3200 (NH₂), 2190 (CN). NMR (CDCl₃) δ : 0.98 (3H, t, CH₃CH₂-, $J=8$ Hz), 1.24 (3H, s, CH₃C-), 1.64 (2H, q, CH₃CH₂-, $J=8.0$ Hz), 1.76 (3H, d, CH₃CH=, $J=8$ Hz), 2.40 (2H, s, -CH₂-), 4.98 (2H, broad, NH₂), 5.72 (1H, q, -CH=, $J=8$ Hz). MS m/e : 240 (M⁺).

Treatment of the above filtrate did not give the corresponding reduction product.

Reaction of 1-Phenylethylidenemalononitrile (V) with TEAF—To a solution of 6.4 g (0.038 mol) of V in 80 ml of DMF, 10.4 g (0.12 mol based on HCO₂H) of TEAF was added in one portion. The reaction mixture was heated at 74–75° with stirring for 3 hr. Evolution of a slight amount of CO₂ was observed. Treatment of the reaction mixture by the same procedure described above gave yellow crystals. Recrystallization from acetic acid gave yellow needles of 2-imino-6-methyl-4,6-diphenyl-3-cyclohexene-1,1,3-tricarbonitrile (VI), mp 202–204° (lit.⁹) 209–210°, yield, 4.0 g (51%). Anal. Calcd. for C₂₂H₁₆N₄: C, 78.55; H, 4.79; N, 16.66. Found: C, 78.27; H, 4.81; N, 16.44. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 3230 (NH), 2185 (CN). NMR (DMSO-*d*₆) δ : 1.82 (3H, s, CH₃), 3.66 (2H, ABq, -CH₂-, $J=20$ Hz, H_A-H_B=44 Hz), 7.40–7.80 (10H, m, aromatic protons), 9.96 (1H, s, NH). MS m/e : 336 (M⁺).

Benzene extraction of the above filtrate and evaporation of benzene followed by distillation of the residual oil under reduced pressure gave colorless oil of (α -methylbenzyl)malononitrile, bp 100–105°/0.07 mmHg, yield, 1.05 g (16%). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 2250 (CN). NMR (CDCl₃) δ : 1.62 (3H, d, CH₃CH, $J=1.1$ Hz), 3.44 (1H, p, CH₃CH, $J=1.1$ Hz), 3.88 (1H, d, >CHCH(CN)₂, $J=1.0$ Hz), 7.39 (5H, s, C₆H₅).

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